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FOREWORD

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Introduction

Increasing numbers of older women with breast cancer are receiving breast-conserving surgery (BCS) without axillary dissection. While such an approach appears efficacious in randomized controlled trials, there is concern that it contributes to higher breast cancer mortality in the community. Our aim was to determine whether failure to perform axillary dissection is associated with decreased survival in women with early-stage breast cancer. We studied 26,290 women with early-stage breast cancer aged ≥ 25 in 1983-1993 who received BCS, using data from the Surveillance, Epidemiology and End Results Program and Medicare.

Body

Key Research Accomplishments

The findings of this study so far can be summarized as follows. First, substantial numbers of older women receiving breast-conserving surgery do not receive axillary dissection.^{1,2} Second, of those women not receiving axillary dissection, most also do not receive either adjuvant radiation therapy or chemotherapy.³ In other words, they receive no therapy directed at occult cancer in the axillary nodes. The percentage of older women who receive no therapy to their axillary nodes has been steadily increasing over the past decade.^{1,4} Third, patients receiving breast-conserving surgery without axillary dissection experience significantly worse survivals than those who do, after controlling for other factors known to affect survival. Finally, there is an interaction between receipt of axillary dissection and radiation therapy on survival, such that women who receive either axillary dissection or radiation therapy experience similar survivals to those who receive both axillary dissection and radiation, while women who receive neither treatment experience substantially poorer survivals.

Reportable outcomes

Table 1 presents the percentages of women receiving breast-conserving surgery (BCS) with or without axillary dissection by patient and tumor characteristics. Overall, 27% of all women with early stage breast cancer who underwent BCS did not receive axillary dissection as part of initial surgical treatment. Older women, unmarried women and those with very small (<0.5 cm) or very large tumors (≥ 4.0 cm) were less likely to receive axillary dissection. The data on the percentages receiving axillary dissection by stage are misleading, because the major means of distinguishing regional from local stage is by axillary dissection. Thus there is a misclassification bias of underreporting regional stage tumor in women without axillary dissection. Because of this, in the survival analyses we control for tumor size rather than stage.

As discussed in the Introduction, axillary dissection may be less important if patients not receiving axillary dissection receive adjuvant radiation therapy or chemotherapy.^{5,6} We investigated this issue in women aged 65 and over and diagnosed with early stage breast cancer between 1991 and 1993 using the SEER-Medicare linked data, which provides information on radiation therapy, chemotherapy, and comorbid conditions.⁷ Table 2 presents the percentage of women receiving radiation and chemotherapy as a function of receipt of axillary node dissection.

Of women receiving BCS without axillary dissection, nearly two-thirds (62%) also did not receive radiation therapy. The great majority of these older women (98%) did not receive chemotherapy. Women not receiving axillary dissection actually had a lower chance of receiving radiation or chemotherapy than those receiving axillary dissection.

Table 3 presents the interaction between axillary dissection and receipt of radiation therapy on mortality of women aged 65 and older with early stage breast cancer. Women receiving neither axillary dissection nor radiotherapy were at a significantly higher risk for death, compared to those who received both axillary dissection and radiation therapy. Women receiving either radiation alone without axillary dissection, or axillary dissection without radiation were not at significantly higher risk for death, after adjusting for patient and tumor characteristics.

Conclusions

In conclusion to date, the combination of no axillary dissection plus no radiation after BCS is associated with an unacceptably high level of deaths from breast cancer. The lack of improvement in the past two decades in survival of older women with breast cancer may be explained in part by the increasing use of treatments that do not address potential tumor in axillary nodes. Further research will be performed to look at social economic factors in relation to the effect of axillary node dissection on clinical outcomes.

From the performance of this study, a great deal has been learnt about using the large databases such as Medicare claims for research. Considerable experience has been gained in using Medicare data to explore comorbidity status and treatment procedures, and in performing survival analyses.

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Appendix

Appendix 1. Tables 1-3.

Table 1. Receipt of axillary dissection by women with breast cancer who received breast conserving surgery (BCS) between 1988 and 1993 in 9 SEER areas, by patient and tumor characteristics

| Patient and tumor characteristics | Number (%) of women receiving BCS* without axillary dissection | Number (%) of women receiving BCS* with axillary dissection | Total |
|-----------------------------------|--|---|--------------|
| Age (years) | | | |
| 25-54 | 931 (10.2) | 8173 (89.8) | 9104 |
| 55-64 | 835 (15.2) | 4674 (84.8) | 5509 |
| 65-74 | 1604 (26.0) | 4573 (74.0) | 6177 |
| 75+ | 3421 (62.2) | 2079 (37.8) | 5500 |
| Race | | | |
| White | 6021 (26.0) | 17145 (74.0) | 23166 |
| Black | 463 (26.1) | 1313 (73.9) | 1776 |
| Other | 252 (20.9) | 955 (79.1) | 1207 |
| Unknown | 55 (39.0) | 86 (61.0) | 141 |
| Marital status | | | |
| Married | 2588 (17.4) | 12276 (82.6) | 14864 |
| Unmarried | 3866 (36.0) | 6876 (64.0) | 10742 |
| Unknown | 337 (49.3) | 347 (50.7) | 684 |
| Cancer stage | | | |
| Stage I | 5143 (28.7) | 12750 (71.3) | 17893 |
| Stage IIA | 1442 (22.4) | 4998 (77.6) | 6440 |
| Stage IIB | 190 (10.8) | 1564 (89.2) | 1754 |
| Stage II, NOS † | 16 (7.9) | 187 (92.1) | 203 |
| Tumor size (cm) | | | |
| <0.5 | 472 (38.9) | 743 (61.1) | 1225 |
| 0.5-<1.0 | 1294 (25.0) | 3883 (75.0) | 5177 |
| 1.0-<2.0 | 2857 (23.9) | 9089 (76.1) | 11946 |
| 2.0-<3.0 | 1362 (25.2) | 4053 (74.8) | 5415 |
| 3.0-<4.0 | 466 (30.4) | 1066 (69.6) | 1532 |
| 4.0+ | 324 (40.4) | 478 (59.6) | 802 |
| Unknown size | 16 (7.9) | 187 (92.1) | 203 |
| Total | 6791 (25.8) | 19499 (74.2) | 26290 |

* BCS denotes breast-conserving surgery.

† NOS - not specified.

Table 2. Receipt of radiation therapy and chemotherapy in women aged 65 and older who underwent breast conserving surgery in 1991 through 1993, with or without axillary node dissection*

| Surgical treatment categories | Number of patients | Number (%) of women receiving radiation therapy † | Number (%) of women receiving chemotherapy ‡ |
|---|---------------------------|--|---|
| breast conserving surgery without axillary dissection | 2215 | 853 (38.5) | 52 (2.4) |
| breast conserving surgery with axillary dissection | 2974 | 2673 (85.9) | 163 (5.2) |

* For women with early stage (local or regional) breast cancer diagnosed between 1991 and 1993 from the SEER-Medicare linked database.

† Radiation therapy was defined if SEER data indicated so or if there were Medicare claims for radiation therapy within 4 months after diagnosis of breast cancer.

‡ Chemotherapy was defined if patients had at least one Medicare claim for chemotherapy within 12 months after diagnosis.

Table 3. Interaction between receipt of axillary dissection and radiation therapy on breast cancer survival in women aged 65 and older with early stage breast cancer, 1991-1993

| Variables | Number of patients (n=5328) | Hazard ratio for 3-year breast cancer specific mortality (95% CI) † |
|--|-----------------------------|---|
| Patients receiving BCS, by receipt of axillary dissection (Ax) and radiation (XRT)* | | |
| No Ax + no XRT | 1362 | 1.76 (1.24-2.49) |
| No Ax + XRT | 853 | 1.11 (0.74-1.68) |
| Ax + no XRT | 440 | 1.00 (0.59-1.70) |
| Ax + XRT | 2673 | 1.00 |
| Other key risk factors in the model | | |
| Age (years) | | |
| 65-69 | 1287 | 1.00 |
| 70-74 | 1415 | 1.03 (0.69-1.53) |
| 75-79 | 1189 | 1.02 (0.67-1.54) |
| 80+ | 1437 | 1.15 (0.76-1.74) |
| Tumor size (cm) | | |
| <0.5 | 264 | 1.00 |
| 0.5-<1.0 | 1252 | 1.11 (0.42-2.93) |
| 1.0-<2.0 | 2419 | 2.07 (0.84-5.12) |
| 2.0-<3.0 | 968 | 3.51 (1.40-8.77) |
| 3.0-<4.0 | 255 | 6.76 (2.62-17.44) |
| 4.0+ | 138 | 5.50 (2.00-15.12) |
| Unknown size | 32 | 2.52 (0.89-7.09) |
| Comorbidity index scores ‡ | | |
| No Medicare claims | 344 | 0.82 (0.44-1.54) |
| 0 | 3616 | 1.00 |
| 1 | 637 | 1.53 (1.06-2.22) |
| 2 | 323 | 1.76 (1.11-2.79) |
| 3+ | 408 | 2.05 (1.37-3.05) |

* BCS (breast-conserving surgery), No Ax (no axillary dissection); no XRT (no radiation therapy); Ax (axillary dissection); XRT (radiation therapy).

† Hazard ratios (95% confidence interval), adjusted for the variables listed in the table and also adjusted for marital status (married, unmarried and unknown), race (white, black, and other), and 9 SEER areas.

‡ Comorbidity was assessed by a validated algorithm^{29,30} using Medicare claims.

Appendix 2. Abstract.

Abstract was presented at the Society for Epidemiologic Research annual meeting, Seattle, WA, June 15-17, 2000; and published in the Am J Epidemiol 2000;151(suppl):S64.

S64 SER Abstracts

THE EFFECT OF AXILLARY NODE DISSECTION ON SURVIVAL IN WOMEN WITH EARLY STAGE BREAST CANCER. XL Du,* JL Freeman, AB Nattinger, and JS Goodwin (University of Texas Medical Branch, Galveston, TX 77555)

Increasing numbers of older women with early stage breast cancer are receiving breast-conserving surgery (BCS) without axillary dissection. While such an approach appears efficacious in randomized controlled trials, there is concern that it contributes to higher breast cancer mortality in the community. We studied 26,290 women aged ≥ 25 in 1983-93 from the Surveillance, Epidemiology and End Results (SEER) Program and 5,328 women aged ≥ 65 in 1991-93 from SEER-Medicare linked data, who had an early stage breast cancer and received BCS. Overall, 27% of women aged ≥ 25 receiving BCS did not receive axillary dissection, most of whom (74%) were age ≥ 65 . Women receiving BCS with axillary dissection had lower 7-year breast cancer-specific mortality than did those without axillary dissection (Cox proportional hazard ratio=0.53, 95% confidence interval: 0.44-0.63). Women not receiving axillary dissection actually had a lower chance of receiving radiation or chemotherapy than those receiving axillary dissection. Of women receiving BCS without axillary dissection, 62% also did not receive radiation therapy and 98% did not receive chemotherapy. We found an interaction between receipt of axillary dissection and radiotherapy on survival of older women after BCS. Women who received either axillary dissection or radiotherapy experienced similar survivals to those who received both axillary dissection and radiation, while women who received neither treatment experienced poorer survival (hazard ratio=1.76, 1.23-2.52), after controlling for demographics, tumor size and comorbidity. The findings suggested that the combination of no axillary dissection plus no radiation after BCS is associated with an unacceptably high level of deaths from breast cancer. The lack of improvement in the past 2 decades in survival of older women with breast cancer may be explained in part by the increasing use of treatments that do not address potential tumor in axillary nodes.